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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,939	04/12/2004	Tae H. Ji	028750-229	2139

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EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 10/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/821,939	JI ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 19-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III (claims 16-17, drawn to a method of contraception in a female subject comprising administering an agent that modulates CG or CG interaction with exoloop 1, exoloop 2 or exoloop 3 of the LHR, classification dependent on structure of recited "agent", is acknowledged (received 26 September 2005). The traversal was made on several grounds.

On p. 2, 1st paragraph, Applicant points out requirements for restriction as laid out in MPEP 806.04 AND MPEP 806.05, to which the Examiner takes no issue.

Applicants submit on p. 2, 2nd paragraph "that the inventions of Groups I to XVII are closely related and that a proper search of any of the claims should, by necessity, require a proper search of the others. For example, Groups VIII and XVI are so related that the Office identifies them in the same class and subclass (i.e., class 424, subclass 130.1)." Applicants' argument has been fully considered, but not found to be persuasive for the reasons explained in pages 2-15 of the last office action (mailed 23 August 2005). Briefly, Groups I-VI, IX-XIV and XVII are unrelated methods. Groups are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP 806.04, MPEP 808.01). Regarding Groups VIII (drawn to a composition comprising an antibody that binds to CG and prevents CG from interacting with the exoloop 1, exoloop 2 or exoloop 3 of LHR) and XVI (drawn to a composition comprising an antibody

capable of modulating FSH activity by preventing interaction of FSH with the exoloop 1, exoloop 2 or exoloop 3 domain of the FSHR), Applicants argue that because these inventions have the same classification they should be searched together. However, they because they are drawn to antibodies, however, much of the searching in biotechnology areas are done in non-patent literature, which is unclassified, and because they are drawn to different antibodies, they are different products, and there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. 806.05 for inventive groups that are directed to different products. Finally, Applicants' disclosure states on p. 76, 1st paragraph, "The K^{583} substitution enhanced the binding affinity of LHR but the corresponding Ala substitution impaired that of FSHR," thus suggesting that the mechanism of modulating FSH and LH activity are different, and that modulators of FSH-FSHR interaction would differ from modulators of LH/CG-LHR interaction. Thus, the Groups VIII and XVI are drawn to different compositions, and should be restricted.

Applicants also submit on p. 2, 2nd paragraph that Groups I-XVII share the "special technical feature of relating to modulating gonadotropin hormones and related gonadotropin hormone diseases." The instant application was filed under 35. U.S.C. 111, so the special technical feature standard does not apply to this case. In order for the unity of invention and special technical features rules to apply, an application must be filed under 35 U.S.C. 371 (i.e., international application—see Chapter 1800 of the MPEP, especially, DETERMINATION OF "UNITY OF INVENTION.) For U.S. applications, see 37 CFR 1.141:

Different inventions in one national application.

(a) Two or more independent and distinct inventions may not be claimed in one national application...

Applicants also submit on p. 2, 2nd paragraph, that "all of the claims can be searched simultaneously, and that a duplicative search, with possibly inconsistent results, may occur if the restriction requirement is maintained, particularly where the groups comprise the same class, subclass." This argument has been fully considered, but not found to be persuasive. First, much of the searching in the biotechnology area is in the non patent literature, which is unclassified. Second, a search in a typical invention requires the consideration of 200-2000 (or more) prior art documents, and the analysis of each document must be accurate and expeditious. Searching 17 inventions in one application constitutes a severe administrative burden, and the danger to the public is that valid prior art may be missed, which might lead to an improperly prosecuted patent or piecemeal prosecution. Applicants' disclose that the mechanism of modulating FSH and LH activity is be different, and for that reason, modulators of FSH-FSHR interaction would differ, so searching any methods drawn to modulation of LH/CG-LHR interaction would differ from those drawn to modulation of FSH-FSHR interaction. Furthermore, the reproductive systems of males and females differ at the anatomical and molecular level, thus searching inventions drawn to male disorders is not coextensive with searching inventions drawn to female disorders.

Regarding the species election requirement, Applicant's election with traverse of Stimulation of development of the female gonads, follicles, and maturation of oocytes, Tissues and Cells and Diseases is acknowledged. As Applicant states, the elected

invention (Group III) does not recited any of the elected species, and thus, does not apply.

Applicants quote case law on p. 3, 2nd paragraph from In re Weber, 580 F.2d 455,198 USPQ 328 (CCPA 1978), which refers to the impropriety of restriction within claims, however the quotation is misplaced in this instant case. In U.S. applications it is improper to restrict within a single claim, but not between different **inventions**. An applicant may claim more than one species of an invention, not to exceed a reasonable number, in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form (1.75) or otherwise include all the limitations of the generic claim. However, this would only hold once the generic claim is held allowable.

Applicants argue that on p. 3, 3rd paragraph that regarding Markush claims, that it is improper for the Office to refuse to examine that which applicants regards as their invention, unless the subject matter lacks unity of invention." The MPEP 803.02 states:

> If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the Examiner must examine all the members of the Markush group in the claim on the merits...

In the instant case, since the elected claims are generic, it is not necessary to make a species election. However, since applicant did make a species election, (stimulation of development of the female gonads, follicles, maturation of oocytes) from the group Stimulation of Hormones, Tissues, Cells (stimulation of progesterone, androgen and estrogen stimulation; stimulation of development of the male gonads; stimulation of development of the female gonads, follicles, maturation of oocytes; stimulation of development of the placenta; stimulation of development of the sperm; growth of

cells/tissue) are not so closely related that a search and examination of the entire list could be made without serious burden. This list encompasses different hormones, developmental pathways, anatomies and physiologies at the organ, tissue and molecular level. Success with one does not predict success with another.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1-15 and 19-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 26 September 2005.

Specification

The disclosure is objected to because of the following informalities: "glycosylated" is misspelled on p. 3, 1st paragraph. Appropriate correction is required.

The disclosure is objected to because of the following informalities: "identified" is misspelled on p. 8, 3rd paragraph). Appropriate correction is required.

The disclosure is objected to because of the following informalities: there are typos on p. 57, 2nd paragraph ("a subunit" instead of "α subunit"); p. 63, 2nd paragraph ("FSH aα" instead of "FSH α"); p. 64, 2nd paragraph ("PLCb" instead of "PLCβ" and "Ips" instead of "IPs"); p. 68, 1st paragraph ("b" and "a" instead of "β" and "α"). Appropriate correction is required.

Claim Objections

Claims 16 and 17 are objected to because of the following informalities: the claims are not limited to the scope of the invention, drawn to a method of contraception in a ***female*** subject comprising administering an agent that modulates CG or CG interaction with exoloop 1, exoloop 2 or exoloop 3 of the LHR. Claims 16 and 17 are not limited to females. Appropriate correction is required.

Claim Rejections - 35 USC § 112 – 1st paragraph (Enablement)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants claim a method of contraception comprising administering to a subject an amount of agent effective at preventing conception. To successfully prevent an outcome, a method must stop an outcome from occurring 100% of the time. No method of contraception (outside of hysterectomy) prevents pregnancy in every case (See Trussell J. Contraceptive failure in the United States. Contraception. 2004 Aug;70(2):89-96). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy

the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. It was known in the art at the time of application there was still no known 100% effective contraception outside of surgical sterilization. Regarding predictability within the art of contraceptive drug development, see In re Marzocchi:

> [I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. ***This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles.*** Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

A 100% effective method of contraception comprising administration of any "agents" was not known in the art at or around the time the application was filed. (See Trussell J. Contraceptive failure in the United States. Contraception. 2004 Aug;70(2):89-96). The specification gives no direction or guidance as to the identity of a 100% effective contraceptive method comprising administration of agents, nor are there any working examples.

Furthermore, to the extent that the specification intends to reduce the incidence of conception, the scope of the word "agent" is not enabled by the disclosure. The claims recite a method of contraception comprising administering to a subject an amount of agent effective at preventing conception. An agent that inhibits CG activity, wherein said agent is CG, a biologically active fragment thereof, or other synthetic or natural compound encompasses a vast breadth of possible agents, many of which are yet undiscovered. The development of contraceptive methods comprising administration of "agents" encompasses drug discovery and development, however, it also encompasses protein, gene therapy, nutriceuticals, and nearly anything under the sun one could administer to reduce the incidence of conception. Assuming a reasonable interpretation of the claims and that the Applicant meant a pharmaceutical agent, drug discovery is a labor intensive and expensive undertaking, in spite of recent developments in high throughput screening, rational drug design and combinatorial chemistry. According to Swartz and Babelnick, (2002, Perspect Sex Reprod Health, Current Contraceptive Research, 34(6):310-6), research on and development of novel contraceptives has not kept pace with the growing need, and financial, legal and political pressures is a barrier to development of new contraceptive products in the United States (see p. 31, column 2, 2nd paragraph and p. 315, column 1, 2nd paragraph). Applicants contemplate possible agents that would inhibit CG interaction with exoloops 1, 2 or 3 of the LHR (polypeptides, nucleic acids, rDNA molecules for polypeptides) on pps. 25-33, and methods for ***identifying*** agents that modulate gonadotropin activity are contemplated on pps. 39-44, however, well known assays in the art for ***discovering***

agents are not equivalent to a positive recitation of how to make said agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Rather, the disclosure teaches how to discover such agents. This is equivalent to presenting the public a method of discovering agents that have a certain effect, and then obtaining rights for them. These claims fail the "how to make" prong of 35 U.S.C. 112 first paragraph.

Due to the large quantity of experimentation necessary to determine which of the broadly claimed agents block CG activity, furthermore, the extreme unliklihood that such an agent would **prevent** conception, the lack of direction/guidance presented in the specification regarding how to make said agents, the absence of working examples directed to said agents, the complex nature of the invention, the contradictory state of the prior art (see Swartz and Babelnick), the unpredictability of the effects of mutation on protein structure and function (see discussion above and recited references), and the breadth of the claims which fail to recite limitations on agents that block CG activity, undue experimentation would be required of the skilled artisan to make the claimed invention in its full scope.

Claim Rejections - 35 USC § 112 – 1st paragraph (Written Description)

Claims 16, 17 and 18 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a method

of contraception in a female subject comprising administering an agent, wherein the agent is defined in the claims by activity alone. However, there is no description of the agent itself in the specification, other than CG itself. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in claims 16 and 18 is a functional requirement. Claim 17 recites that the agent is CG or a biologically active fragment thereof, or other synthetic or natural compound. Since this encompasses any structure that has the required activity, it does not define any structure. While a CG protein could be made, there is no recitation of what constitutes biologically active fragments or other synthetic or natural compounds. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed agents, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence of CG, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

Claims 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Talwar et al. (Proc. Natl. Acad. Sci. 1994. A vaccine that prevent pregnancy in women. 91:8532-8536). Talwar et al. teach a composition comprising a biologically active fragment of CG (βhCG) that neutralizes the bioactivity of hCG and reduces incidence of

conception. Although the mechanism of action of hCG interaction with exoloop 3 of the LHR was not known to the authors, the discovery made by Applicant does not render an old composition or method patentable.

> "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the< claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

For further explanation, see MPEP 2112: (I. Something which is old does not become patentable upon the discovery of a new property). For this reason, Applicants' discovery of a previously unknown property of hCG-LHR interaction does not impart novelty or nonobviousness to the method of contraception in a female subject comprising administering an agent, wherein the agent is CG, a biologically active fragment thereof or other synthetic or natural compounds. The reference teaches exactly the method steps recited in the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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ELIZABETH KEMMERER
PRIMARY EXAMINER